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Docket No.: 5(446-20005.20/
0070)6/D1150-6US
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFIC E

In re Patent Application of:
David LAM et al.

Application No.: 09/888,224 Confirmation No.: 8097

Filed: June 22, 2001 Art Unit: 1634

For: ENDOGLUCANASES, NUCLEIC ACIDS ENCODING THEM AND METHODS FOR MAKING AND USING THEM (As Amended) Examiner: Jehanne Souay: Sitton

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION UNDER 37 C.F.R. § 1.132

Sir:

1. I, Jay Short, am a co-inventor with David E. Lam and Eric J. Mathur, on the above-identified patent application.

2. I am an expert in the field of molecular biology and enzyme develo ment and was an expert at the time of the invention. I am presently employed as CEO and as a rese: rch scientist at Diversa Corporation, San Diego, CA, assignee of the above-referenced patent appli cation. My resume is attached as documentation of my credentials.

3. I declare that at the time of the invention it would not have required any knowledge or guidance as to which specific structural elements (including, e.g., doma in structures, location active sites, interaction with co-factors or regulatory molecules, secondary ar d tertiary

structure) correlate with endoglucanase activity to create variants of the exemplary endoglucanase of the invention and test the variants for a desired endoglucanase activity. It would no have been necessary for the skilled artisan to know or predict beforehand which specific regions or structural elements of an endoglucanase were necessary for function or activity to routinely generate the genus of endoglucanase-encoding nucleic acids of the invention. At the time of the invention, methods for making and screening endoglucanases were sufficiently comprehensive and routine to predictably generate a genus of endoglucanase-encoding sequences without need of knowing which specific regions or structural elements of a sequence or structure affected function or activity. Methods known at the time of the invention for modifying nucleic acid and polypeptide sequences in combination with high through-put enzyme (e.g., endoglucanase) screening assays made methods that required previous knowledge of structural elements necessary for enzymatic activity obsolete and unnecessary. High through-put enzyme screening methodologies known at the time of the invention (including *in vivo* and *in vitro* nucleic acid expression and enzyme (endoglucanase) screening protocols) made methods that required previous knowledge of protein structure, including secondary or tertiary structure, active site sequences, and the like obsolete and unnecessary. Using methods known in the art at the time of the invention it would not have been necessary to understand which specific regions of enzyme structure (e.g., domain structures, active sites, secondary and tertiary structure) could, or could not, be modified to generate the genus of nucleic acids of the invention without undue experimentation. The specification provided sufficient guidance to one of ordinary skill in the art to make and use the genus of endoglucanase-encoding nucleic acids to practice the invention.

4. However, if the skilled in the art at the time of the invention elected to use elements of enzyme structure for guidance in designing and making variants, using the teaching of the specification the artisan had many sources of direction to understand the structure of endoglucanases to have direction and guidance in determining which amino acid residues could be substituted, deleted or inserted into a nucleic acid to obtain structural and functional variants of an endoglucanase. For example, the specification provides guidance as to what base and residue

changes could be made to make the genus of endoglucanase-encoding nucleic acids of the invention; see, for example, the paragraph from line 31, page 10 to line 16, page 11, and, page 51, lines 16 to 24, of the specification. Direction to the skilled artisan as to which amino acid residues can be substituted, deleted or inserted into a nucleic acid to obtain structural, and functional homologues of an enzyme could also be found in the art at the time of the invention. For example, Dominguez (1996) "The crystal structure of a family 5 endoglucanase mutant in complexed and uncomplexed forms reveals an induced fit activation mechanism," J. Mol. Biol. 257(5):1042-1051, describes the crystal structure of an endoglucanase; Ducros (1995) "Crystal structure of the catalytic domain of a bacterial cellulase belonging to family 5", Structure 3(9):939-49, describes the crystal structure of the catalytic domain of an endoglucanase; Davies (1995) "Structures of oligosaccharide-bound forms of the endoglucanase V from *Humicola insolens* at 1.9 A resolution," Biochemistry 34(49):16210-20, describes the crystal structures of an endoglucanase in various forms; to name only a few examples.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Respectfully submitted

Date: February 7, 2005

Jay Short

sd-213023